REMARKS

Claims 1-24 have been rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Published Patent Application No. 2002/0099302 to Bardy (hereinafter "Bardy") in view of U.S. Patent No. 5,978,751 to Pence et al. (hereinafter "Pence"). Claims 4 and 21 have been canceled thereby obviating the rejection of these claims. Applicants respectfully traverse this rejection as to the remaining claims.

To establish a prima facie case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); MPEP 2143.

Here, the Examiner has failed to establish a prima facie case of obviousness because Bardy and Pence independently or in combination do not teach or suggest all the claim limitations of claim 1-3, 5-20, and 22-24. Applicants respectfully submit neither Bardy nor Pence is even remotely concerned with continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment, as required by claims 1-3, 5-20, and 22-24. It is well established that the Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

Applicants submit that the only the present invention teach or suggest a method and system of continuously analyzing trial data of an ongoing blinded clinical trial utilizing multi-arm study. None of the prior art teaches such analysis while the blinded clinical trial is still ongoing because of the fear of compromising the integrity the trial data and thereby jeopardizing the veracity of the blinded clinical trials. The ongoing blinded clinical trial can be compromised if the source of the data is revealed or can be determined (i.e., the trial data is associated with a particular study arm). Millions of dollars spent on clinical trials can be wasted if the integrity of the blinded clinical trials is compromised. All of the prior art systems and methods describe analyzing the trial data only after the clinical trials have ended. That is, under the prior art system and method, potential positive or negative effects of a drug under study will go unnoticed until the clinical trial is completed. The present system and method continuously analyzes the trial data for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment. A statistically significant event occurs when the result of the statistical analysis exceeds a predetermined threshold. For example, if the drug under study has a high toxicity level, then it would be extremely valuable to identify such negative effect of the drug as earliest possible to end the clinical trial. Only the present invention teaches or suggests identifying such potential positive or negative effects while the blinded clinical is ongoing without compromising the integrity and the blindness of the clinical trial. Because of this and other advantages of the present invention, the assignee of the present application is currently marketing and selling products/services incorporating various embodiments of the present invention with great success.

Whereas, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing method and

system for testing magnetic disk drives. Applicants respectfully submit that neither Bardy nor Pence is not even remotely related to clinical trials and is not concerned with maintaining the secrecy of the collected data. In fact, Bardy must know the source of the data to determine if the patient will or is experiencing congestive heart failure and Pence must know the source of the data to determine which manufacturing station is cause of the device failures.

"To imbue one of ordinary skill in the art with knowledge of the present invention, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim of the insidious effect of hindsight syndrome, wherein that which only the inventor taught is used against the teacher." W.L. Gore & Assoc. v. Garlock, Inc., 721 F.2d 1540, 1553 (Fed. Cir. 1983). In the present case, none of the references teach or suggest continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment, as required by claims 1-3, 5-20, and 22-24.

Applicant respectfully submits that neither Bardy nor Pence teach or suggest any of the steps required in amended independent claim 1 (and similarly any of the steps in amended independent claim 12 and any of the executions performed by the analysis program in amended independent claim 18):

(1) "accessing a trial database comprising trial data of subjects in an ongoing blinded clinical trial comprising a multi-arm study." In fact, paragraph [0009] in Bardy, cited by the Examiner, merely describes accessing patient care records. Contrary to the Examiner's assertion, Bardy does not teach or suggest accessing a trial database of an ongoing blinded clinical trial where the data must be accessed without comprising the integrity of the blind. That is, the clinical trial data must be accessed without revealing the source of the data (i.e., which study arm, the data was from). Whereas, the source of

the data must be known in Bardy to provide proper care to the patient. It is well established that the Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

(2) "accessing a blinding database." In fact, paragraph [0009] in Bardy, cited by the Examiner, merely describes accessing patient care records. Contrary to the Examiner's assertion, Bardy does not teach or suggest accessing a blinded database which stores subject identifiers and associated study group identifiers. Since neither Bardy nor Pence remotely relates to a clinical trial, neither reference is suggestive of storing such identifiers. It is well established that the Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

(3) "generating a grouped database from the trial database and the blinding database." Contrary to the Examiner's assertion, Bardy does not teach or suggest generating a grouped database because neither is concerned with multi-arm study to determine the efficacy of a particular drug vs. another drug or placebo. It is well established that the Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

(4) "performing a statistical analysis on the accessed trial database without suspending the ongoing blinded clinical trial." In fact, paragraph [0009] in Bardy, cited by the Examiner, merely describes analyzing stored patient measurements and logging any change in patient's condition. Contrary to the Examiner's assertion, Bardy does not teach or suggest performing a statistical analysis on the accessed trial database without suspending the ongoing blinded clinical trial. Since neither Bardy nor Pence remotely relates to a clinical trial, neither reference is suggestive of performing statistical analysis while maintaining the blindness of the clinical trial. It is well established that the

Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

(5) "determining whether the result of the statistical analysis exceeds a predetermined threshold value." In fact, paragraph [0059] in Bardy, cited by the Examiner, merely describes comparing predicted measure value to a threshold. Contrary to the Examiner's assertion, Bardy does not teach or suggest comparing the results of a statistical analysis performing a statistical analysis on the accessed trial database without suspending the ongoing blinded clinical trial. Since neither Bardy nor Pence remotely relates to a clinical trial, neither reference is suggestive of performing statistical analysis for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment while maintaining the blindness of the clinical trial. It is well established that the Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

(6) "if it is determined that the result of the statistical analysis does not exceed the predetermined threshold value, then repeating the steps of accessing, performing and determining while the blinded clinical trial is ongoing." The Examiner admits that Bardy is not suggestive of this step and turns to Pence for allegedly describing this step. However, as noted herein, Pence relates to a manufacturing method and system for testing magnetic disk drives. Since Bardy and Pence remotely relate to a clinical trial, neither is suggestive of repeating the steps of accessing the trial database, performing statistical analysis, and determining whether the result of the statistical analysis exceeds the predetermined threshold value. It is well established that the Examiner cannot use hindsight gleaned from the present invention to modify or reconstruct the prior art reference to render claims unpatentable.

The prior must to be judged based on a full and fair consideration of what that art teaches, not by using Applicants' invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicants' invention. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable. Accordingly, it is submitted that the Examiner has succumbed to the lure of prohibited hindsight reconstruction.

Not only does Bardy and Pence independently or in combination fail to teach or suggest continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study, as required by claims 1-3, 5-20, and 22-24. The combination of Bardy and Pence fails to teach or suggest any of the claimed steps of accessing a trial database, accessing a blinding database, generating a grouped database, performing a statistical analysis, determining, and repeating, as required by amended independent claim 1 (and similarly independent claims 12 and 18). Hence, applicants respectfully submit that the Examiner has failed to establish the basic requirements of a *prima facie* case of obviousness for claims 1-3, 5-20, and 22-24.

Further, the claimed invention defined by the claims eliminates the shortcomings and disadvantages encountered with the prior art. Specifically, the claimed invention continuously analyzes trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study. None of the cited references are directed to the problem solved by the present invention. It is undeniable that neither Bardy nor Pence is even remotely concerned with the problem of continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment. The mere fact that the prior art can be

modified does not make the modification obvious. Here, as noted herein, the Examiner's primary reference (Bardy) relates to solving a completely different problem of diagnosing and monitoring congestive hear failure in a patient; and the secondary reference (Pence) relates to solving another completely different problem of providing manufacturing system and method for testing devices, such as magnetic disk drives.

Absent evidence that the specific problem of continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study was even recognized by the prior art, there can be no finding that the invention as a whole would have been obvious. As stated by the PTO Board of Appeals in Ex parte Breidt and Lefevre, 161 U.S.P.Q. 767, 768 (1968), "an inventive contribution can reside as well in the recognition of a problem as in a solution". It further appears that the conclusion reached by the Board of Appeals in Ex parte Minks, 169 U.S.P.Q. 120 (1969), is here in point. There, the Board concluded that "[a]ppellant having discovered the source of the problem and solved the same . . . he is... entitled to patent protection". Id. at 121.

Since applicant has recognized a problem not addressed by the cited prior art and solved that problem in a manner not suggested by either Bardy or Pence, the basis for patentability of the claims is established. See In re Wright, 6 U.S.P.Q. 2d, 1959, 1961-1962 (Fed. Cir. 1988). There, the CAFC relied upon previous decisions requiring a consideration of the problem facing the inventor in reversing the Examiner's rejection. "The problem solved by the invention is always relevant". Id. at 1962. See also, In re Rinehart, 189 U.S.P.Q. 143, 149 (C.C.P.A. 1967), which stated that the particular problem facing the inventor must be considered in determining obviousness.

In view of the foregoing, it is respectfully submitted that one of ordinary skill in the art, after reading and understanding Bardy, would not even turn to Pence and if she

did, she would not understand how or why Bardy's congestive heart monitoring system s should be combined with Pence's manufacturing testing system. Even if such combination is made, the resulting combination will not teach or suggest the present invention.

Therefore, the Examiner has again failed to establish a *prima facie* case of obviousness because these references independently or in combination thereof fails to solve the problem of continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study. Accordingly, Applicants respectfully request this rejection be withdrawn.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 50-0624, under Order No. NY-MSI 203-US from which the undersigned is authorized to draw.

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Respectfully submitted,

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